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Nanochannel-Based Electroporation Assisted Tissue Reprograming and Repair

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Recent advances in *in vitro* nuclear cell reprogramming have opened up the possibility for the development of patient specific therapies, and are thus a great leap forward in translational regenerative medicine. New evidence suggests that nuclear cell reprogramming can also be induced *in vivo*, which could potentially facilitate the transition from the lab bench to the clinic in some cases. However heavy reliance on viral methods is in conflict with clinical applications. Therefore, to realize the full potential of *in vivo* reprogramming, a safer, more efficient and better-controlled approach for the delivery of complex combinations of reprogramming factors is needed. Our newly developed nanochannel electroporation (NEP) patch technology allows for non-viral in vitro as well as *in vivo* gene delivery in a targeted, controlled and benign manner, which is not attainable by existing technologies. Plasmids encoding for specific reprogramming transcription factors were used as model cargo. Tissue transfection was characterized by *in vivo* imaging tool (Fig. 1). A specific cocktail of transcription factors Etv2, Fli1 and Foxc2 (EFF) was found to be enhanced by the transdifferentiation of adult fibroblast into functional reprogrammed endothelial cells both *in vitro* (Fig. 2) as well as *in vivo* where ischemic tissues re-gained significant vascularization (Fig. 3) following NEP-based delivery of such reprogramming factors. Here we explored the tissue repair by reprogramming amenability of adult skin fibroblast to endothelial cells by the use of electrotransfection technology.

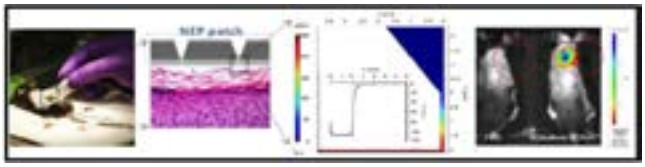

Figure 1: In vivo transfection of tagged DNA by non-viral nanoelectroporation approach. Electrotransfection of TFs was done on mouse skin with nanofabricated chip and validated with in vivo imaging system.

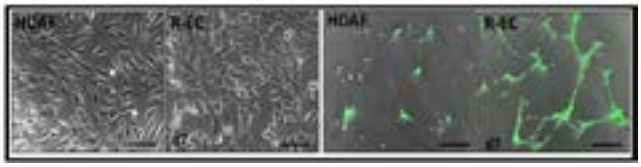

Figure 2: Nanoelectroporation of EFF cause dermal fibroblast to reprogram into endothelial cells by (A) by adapting cobblestone morphology of endothelial property. (B) functionally by showing capillary like tube formation on matrigel.

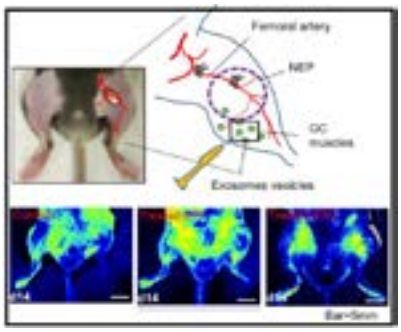

Figure 3: Improvement of ischemic hind limb (A) by pictorial representation of delivery of EFF or exosomes laden with EFF; (B) resulting revascularization of hindlimb within 14 days (Treated–EFF) or exosomes laden with EFF (Treated-EXO) as compared to control. Blood perfusion was evaluated by using laser Doppler blood flow meter of ischemic and non-ischemic limbs.

Biography

Durba Pal recently joined as a faculty in the Center for Biomedical Engineering at Indian Institute of Technology Ropar, India. Her research area is on Tissue Engineering and Regenerative Medicine. After completion of her PhD from India in Molecular Biology, she joined The Ohio State University, Columbus OH, USA, as Post-doctoral Fellow where she began her journey in the field of cellular reprogramming and regenerative medicine. She has discovered the unique cocktail of transcription factors that can be able to convert dermal fibroblasts to endothelial cells when delivered in a simple-to-implement nano-electroporation approach. She had been successful in tissue repairing by *in vivo* reprogramming approach.

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